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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,059	05/28/2002	Henry Yue	PF-0681 USN	4670

22428 7590 01/23/2006

FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
WEGERT, SANDRA L	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 01/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,059	YUE ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *1,2,7,9 and 12-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-6,8,10 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/29/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, and/or Claims

The Information Disclosure Statement, sent 29 December 2005, has been entered into the record. Applicant's election of Invention II with the secondary election of SEQ ID NO: 57, is acknowledged. In addition, Applicants argued that Groups I and II should be rejoined because they share a special technical feature ("Remarks," page 2, 10 November 2005), that being SEQ ID NO: 57, encoding SEQ ID NO: 28.

However, the first claimed invention lacks a special technical feature because it fails to distinguish the claimed invention from the prior art (e.g., Toribara, et al, 1991, J. Clin. Invest., 88:1005-1013, refer to Accession No. AAA59875.1). The prior art discloses immunogenic (biologically active) fragments of SEQ ID NO: 1, one of the SEQ ID NO's recited in Claim 1. For this reason, none of the other claimed inventions can share a special technical feature with the first claimed invention, and Unity is broken. The examiner does agree that appropriate method claims will be rejoined to the elected invention when there is allowable subject matter ("Remarks," page 3, 10 November 2005).

Claims 1, 2, 7, 9, and 12-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected Invention, there being no allowable generic or linking claim.

Claims 3-6, 8, 10 and 11 are under examination in the Instant Application, as reading on SEQ ID NO: 57.

Informalities

Specification

The disclosure is objected to because of the following informalities:

Title

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Appropriate correction of the title is required.

URL's

The disclosure is objected to because it contains browser-executable code. This occurs, for example, on page 18, line 5, for example. All URL's should be removed from the Specification. Applicant may refer to web sites by non-executable name only. See MPEP § 608.01 (p).

Appropriate correction is required.

Claim Rejections/Objections

Claim Objections

Claims 4 and 10 are objected to for reciting non-elected inventions (e.g., SEQ ID NO's other than 57 and 28).

Appropriate correction is required.

Claims 3 and 8 are objected to for depending from withdrawn independent claims.

Appropriate correction is required.

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph, Utility, Enablement

The following is a quotation of 35 U.S.C. 101:

> ***Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> ***The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.***

Claims 3-6, 8, 10 and 11 are rejected under 35 U.S.C. 101 because the claimed invention lacks a specific and substantial asserted utility or a well-established utility.

The claims are directed to a nucleotide which encodes a polypeptide of 320 amino acids, that resembles a human transmembrane receptor/protein (HTMP) (page 58 of Disclosure, for example). However, the Disclosure does not indicate a function for the nucleotide encoding human HTMP in the context of the cell or organism.

No well-established utility exists for newly isolated complex biological molecules. However, the Disclosure asserts the following as credible, specific and substantial patentable utilities for the claimed polynucleotide and polypeptide encoded by the claimed polynucleotide:

1) To produce the HTMP polypeptide and fragments (throughout Disclosure).

2) To produce a variant polypeptide (page 26).

3) For use in receptor localization (sections VIII-XI).

4) In assays to screen for compounds capable of modifying the interaction between receptor and ligand (sections VIII-XI).

5) To make antibodies to the polypeptide encoded by the polynucleotide of SEQ ID NO: 57.

6) In tissue typing (Table 4).

Each of these shall be addressed in turn:

1*) To produce the HTMP polypeptide and fragments.* This asserted utility is credible and substantial, but not specific. Many nucleotide sequences can be used to make polypeptides. However, if the Disclosure discloses nothing specific and substantial about the polynucleotides or polypeptides, both the polynucleotides and polypeptides produced have no patentable utility.

2) To produce a variant polypeptide. This asserted utility is not substantial or specific. Such assays can be performed with any polynucleotide. Further, the Disclosure discloses nothing specific or substantial for a variant nucleotide and polypeptide that might be produced by this method. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

3) For use in receptor localization. This asserted utility is credible, but it is neither substantial nor specific. Probes, ligands and antibodies can be used to detect binding partners of the claimed polynucleotide and disclosed polypeptide; thus, the asserted utility is not specific. Further, the Disclosure does not disclose specific receptor targets. Since this asserted utility is

not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

4) In assays to screen for compounds capable of modifying the interaction between receptor and ligand. This asserted utility is substantial but not specific. Such can be performed for any receptor-ligand pair. Additionally, the Disclosure discloses nothing specific or substantial for the compounds that can be identified by this method.

5) To make antibodies to the polypeptide encoded by the polynucleotide of SEQ ID NO: 57. This asserted utility is substantial, but not specific. Antibodies can be made to any polypeptide. However, if the Disclosure discloses nothing specific and substantial about the polypeptide, then the polypeptide, the polynucleotide encoding the polypeptide and antibodies have no patentable utility.

6) *In tissue typing.* This asserted utility is credible but not substantial or specific. Such assays can be performed with any polypeptide encoded by a polynucleotide; thus, the asserted utility is not specific. Furthermore, the Disclosure discloses a wide range of tissues that express the HTMP polypeptide. Applicant implies that this expression pattern supports a useful function for the HTMP polypeptide. However, patentable utility of tissue typing for the claimed polynucleotide encoding the HTMP polypeptide is not substantial, because one skilled in the art would not readily use the nucleotide sequences for tissue-typing in a real world sense as the protein is not specific to one tissue and is not associated with any disease or disorder. This asserted utility is also not specific because numerous unrelated nucleotide sequences would also show a similar tissue typing pattern. In addition, evidence of mere expression in a tissue is not tantamount to a showing of a role for the polynucleotide of the present invention. It is not clear

if expression of the polynucleotide of the present Invention is correlated with a specific change in physiology, for example, or with a disease state. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

Claims 3-6, 8, 10 and 11 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Claims 3-6, 8, 10 and 11 are directed to an isolated nucleic acid molecule that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 28. The claims also recite a nucleic acid molecule that has a nucleotide sequence comprising the polynucleotide of SEQ ID NO: 57. Further, the claims recite a promoter and sequence comprising the nucleic acid molecule for producing the polypeptide having the amino acid sequence of SEQ ID NO: 28, a recombinant cell, and long fragments of SEQ ID NO: 57. However, the Disclosure does not teach functional or structural characteristics of the polynucleotide or HTMP polypeptide recited in the claims.

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is

considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Bork et al. (1996, Trends in Genetics 12(10): 425-427) who state that functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and that overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Examples from the receptor art demonstrate polypeptides with high homology having a wide-variety of functions in organisms (Ji, et al, 1998, JBC, 273:17299-17302). Even closely-related family members sometimes work very differently and have different specific functions in the organism (Ji, et al, 1998, p. 17302, 3rd paragraph).

Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the Disclosure fails to teach the skilled artisan how to use the claimed polynucleotides to make the biologically active HTMP receptor without resorting to undue experimentation to determine what the specific biological activities of the polypeptide are.

The Disclosure does not teach the skilled artisan how to use the claimed polynucleotides encoding HTMP for any purpose. For example, there is no disclosure of particular disease states correlating to an alteration in levels or forms of the polypeptide such that the claimed polynucleotides encoding HTMP could be used as a diagnostic tool. Therefore, the skilled artisan is not provided with sufficient guidance to use the claimed polynucleotides for any purpose.

Furthermore, the Instant Application does not reasonably provide enablement for various fragments and variants of SEQ ID NO: 57, as encompassed by Claims 3, 10 and 11. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention, nor any fragments or variants of the claimed polynucleotide. Applicants have not made any variants of SEQ ID NO: 57 or 28.

Due to the large quantity of experimentation necessary to determine an activity or property of the disclosed polypeptide such that it can be determined how to use the claimed polynucleotides encoding HTMP and to screen for activity, the lack of direction/guidance presented in the Disclosure regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing that biological activity cannot be predicted based on structural similarity and the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite particular and substantial biological activities, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 USC § 112, first paragraph – Written Description.

Claims 3-6, 8, 10 and 11 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The claims are directed to nucleotide(s) which encode an HTMP polypeptide (see Table 4). Further claim limitations are presented to isolated nucleic acids having at least 90% sequence identity to a nucleic acid encoding the polypeptide of SEQ ID NO: 28, or large fragments of SEQ ID NO: 57. Claims are also presented encompassing vectors and cells comprising nucleic acids having at least 90% sequence identity to SEQ ID NO: 57.

The specification teaches a polynucleotide (SEQ ID NO: 57) and a polypeptide (SEQ ID NO: 28). However, the specification does not teach functional or structural characteristics of all claimed polynucleotides. The description of one polynucleotide encoding an HTMP polypeptide (SEQ ID NO: 28) is not adequate written description of an entire genus of functionally equivalent polynucleotides and polypeptides.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of all claimed polynucleotides and all encompassed HTMP polypeptides, and therefore, would not know how to make or use them. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of

the method of use. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of use. The nucleotide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

To provide evidence of enablement of a claimed genus, the Disclosure must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a partial structure in the form of a recitation of percent identity or large fragments that have not been adequately identified. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the Disclosure does not provide adequate written description of the claimed genus.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only an isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 57 and a polypeptide comprising the amino acid sequence of SEQ ID NO: 28, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description

provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Conclusion: Claims 3-6, 8, 10 and 11 are rejected for the reasons recited above.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SLW
15 January 2006

Eileen B. O'Hara

EILEEN B. O'HARA
PATENT EXAMINER